3

Thresholds of Health Effects for Chemical and Biological Agents

In evaluating potential exposures to CB agents, DoD must consider how to detect and monitor health-relevant exposures to a broad set of CB agents, which will require knowing the dose-responses for these agents. In evaluating the potential use of CB agents, DoD must consider the nature of future deployments and the increasing capabilities of other countries to use CB agents as weapons.

Low-level exposure to chemical agents is unlikely to result in acute effects. However, over the long term, low-level exposure may increase the likelihood of chronic illness. In contrast to high-level exposures for which the severity of effect tends to increase as the level of exposure increases, it is postulated that as low-level chemical exposures increase, the probability of disease increases. These concepts are commonly used to assess risks from exposure to chemical agents but have not been tested for biological agents. Although it is possible to characterize an acute threshold concentration for chemical agents and apply a safety factor that establishes an acceptable low-level exposure, it is difficult to define an acceptable low-level exposure for biological agents.

Characterizing the effects of troop exposures to CB agents will require that research and field data on the effects be immediately available. However, no DoD plan for collecting, storing, and making these data available was described or even referred to during this study. These data must be kept current and made accessible to reseachers, medical personnel, decision makers, planners, and others responsible for protecting deployed troops.

CHEMICAL AGENTS

Deployed personnel face potential exposures to chemical warfare agents at concentrations that can be incapacitating or life threatening; however, they may also be exposed to chemical warfare agents at low levels that are currently not detectable or well monitored. As chemical warfare agents proliferate, the likelihood of in-theater and, possibly domestic, exposure to intentional releases of these agents increases.

In addition to exposure to chemical agents, troops may be exposed to a number of other potentially harmful agents during military deployments. Among these nonwarfare agents are volatile components and combustion products from propellants, explosives, and pyrotechnics (PEP) and a growing number of TICs, including chemicals associated with military materiel, such as pesticides, fuels, lubricants, cleaning agents, solvents, combustion products, chlorine, and other reactive compounds (from chemical storage depots), depleted uranium, and other toxic metals.

Important properties of chemical agents include the physical state at ambient conditions, toxicity, volatility, stability, and transport characteristics (i.e., how rapidly an agent travels or spreads in air, water, or soil). For liquid agents, ingestion, dermal contact, and eye contact are the most likely routes of intake and uptake. For airborne chemicals, uptake is usually respiratory (through inhalation), ocular (absorption by the eyes), or percutaneous (absorption through the skin) (Boyle, 1998a; U.S. Army et al., 1990). For airborne chemical agents, three factors determine the dose received: (1) the concentration of the chemical in the air and the characteristics of any aerosol-phase concentration (particle size distribution and chemistry); (2) the length of time an unprotected individual breathes the contaminated air; and (3) the individual's breathing rate, which is affected by his or her activity level.

The relative toxicity of a chemical agent is expressed either in terms of the lethal dose (*LD*) for a liquid agent or lethal exposure (*LCt*) for a vapor or aerosol agent; or incapacitating dose (*ID*) for a liquid agent or incapacitating exposure (*ICt*) for a vapor or aerosol. These expressions of toxicity are commonly described as median doses:

- LD_{50} is a measure of liquid agent lethality; the dose in milligrams (mg) of liquid agent or mg of agent delivered per kilogram (kg) of body weight expected to kill 50 percent of a group of exposed, unprotected personnel (U.S. Army et al., 1990).
- ID_{50} is the dose in mg or mg/kg of liquid agent expected to incapacitate 50 percent of a group of exposed, unprotected personnel (U.S. Army et al., 1990). In some cases, an ED_{50} is used instead of

the ID_{50}. The ED_{50} is the amount of liquid agent on the skin sufficient to produce severe effects in 50 percent of the exposed population (NRC, 1997c).

- LCt_{50} is a measure of vapor or aerosol agent lethality, which is the product of the concentration and exposure time that is lethal to 50 percent of a group of exposed, unprotected personnel at an assumed breathing rate (active or resting) (U.S. Army et al., 1990). The units commonly used to express the LCt_{50} are mg-min/m^3. If the exposed forces are very active and breathing rapidly, the LCt_{50} would be lower because of the higher breathing rate. The LCt_{50} is based on an assumption of a relatively short exposure time—typically less than an hour—but can often be applied for longer times. The LCt_{50} also varies with the degree of protection provided by masks and clothing, although the standard is based on unprotected personnel. The NRC Committee on Toxicology uses the term EC_{50} instead of LCt_{50}. EC_{50} is the airborne concentration of a chemical agent sufficient to produce the effects of interest in 50 percent of those exposed for 30 minutes (NRC, 1997c). EC_{50} is similar to, but higher than, the immediately dangerous to life and health (IDLH) concept used by the EPA as the maximum concentration of a contaminant to which a person could be exposed for 30 minutes without experiencing any escape-impairing or irreversible health effects.
- ICt_{50} is the incapacitating effect of a vapor or aerosol agent, which is the product of the concentration and exposure time sufficient to disable 50 percent of a group of exposed, unprotected personnel at an assumed breathing rate (active or resting) (U.S. Army et al., 1990). ICt_{50} also decreases as the rate of breathing increases and increases as the level of protection (e.g., clothing, masks) increases.

The allowable exposure level (AEL) is the chemical concentration in air that is safe for continuous exposure during an 8-hour work day/40-hour work week (ERDEC, 1996). The AEL is a general term indicating a level of exposure that is unlikely to result in adverse health effects. The Occupational Safety and Health Administration's (OSHA's) rules call for the use of maximum personal protection until concentrations can be shown to be less than 50 times the AEL.

These measures of effect are useful for defining the types and sensitivity of exposure information to protect against short-term or long-term health effects. In the past, DoD generally focused only on the lethal or incapacitating dose of chemical agents. However, given the concerns of Gulf War veterans about health symptoms and given recent congressional directives that DoD (1) modify its policies and doctrine to protect

personnel from low levels of agents in combination with other exposures, and (2) focus a research program on the effects of low-level exposures, DoD has become concerned about the potential health effects of exposures at lower levels (U.S. Congress, 1994).

Chemical Warfare Agents

Chemical warfare agents are chemical compounds used in military operations that are intended to kill, seriously injure, or incapacitate troops through their physiological effects (U.S. Army and U.S. Marine Corps, 1996). (A summary description of chemical agents of concern to DoD is provided in Appendix B.) A person becomes a casualty of a chemical warfare agent when s/he is affected to a point that prevents or degrades that individual's ability to carry out his/her duties.

Chemical warfare agents are classified as lethal, blister, or incapacitating agents. Lethal nerve agents include choking agents, blood agents, and nerve agents. Blister agents may be lethal, but their primary effect is skin damage. Incapacitating agents (lacrimators, sternutators, and psychochemical agents) cause psychological or mental effects that lead to temporary disability. However, in sufficiently high exposures and doses, incapacitating agents can also be lethal (U.S. Army et al., 1990). As chemical warfare agents proliferate, the likelihood of theater and even domestic exposure to intentional releases of these agents also increases.

Toxic Industrial Chemicals

In addition to traditional chemical warfare agents, deployed troops can be exposed to many other harmful chemicals, from environmental and occupational chemicals to TICs. These harmful chemicals may be a source of low-level exposures; they may even produce a chemical cloud that can degrade mission performance as much as some warfare agents. Toxic chemicals that are commonly used in modern and emerging industrial economies are also commonly used in military operations, and low to intermediate levels of exposure are plausible during a deployment. In addition to having an immediate impact on performance, exposures are believed to contribute to the risk of developing cancer and other serious diseases later in life (EPA, 1986b; Howard, 1989; WHO, 1979, 1982c, 1983, 1993).

The number and likelihood of exposures of U.S. forces to occupational and environmental chemicals are both increasing (GEO-CENTERS and Life Systems, 1997). The literature on the identification, evaluation, and control of human exposures to harmful industrial/commercial chemicals in both occupational and nonoccupational settings is extensive. In

areas where U.S. forces are likely to be deployed, the likelihood of exposures to multiple environmental chemicals is high. Although many industrialized nations have strict controls on the release of industrial chemicals, less-developed nations may not have the political or institutional infrastructure to provide protection from exposures to harmful substances. During military deployments, these exposures could be even higher as a result of the breakdown of local governments, damage to industrial facilities, or the use of operational areas as dumping grounds for hazardous industrial waste.

Detecting and monitoring chemical substances can be very difficult in a deployment setting. In the United States, harmful agents are typically identified for both occupational and environmental assessments. During deployments, these substances must first be identified, which could be difficult because the sources are not likely to be known or well characterized. Thus, a detailed sampling strategy is required to assess environmental levels. In contrast to well characterized emissions data for U.S. occupational and environmental settings, emissions data are sparse during deployment. Appendix B, provides some examples of the types of chemical substances associated with these source categories and gives examples of their sources and emission levels.

Defense personnel may be exposed to large chemical releases from industrial accidents at home or abroad, from deliberate acts of enemy forces or terrorists, from unintentional operational releases, and from natural disasters. Chlorine gas, for example, is used and stored by a large number of industrial-process facilities, especially water treatment facilities, and is also widely used as a reagent in the manufacture of chlorinated organic materials and inorganic chlorides and chlorates. Thus, chlorine storage tanks are likely to be present in an urban or industrial environment. Chlorine is a powerful irritant, both in the upper and the lower respiratory tract. The median lethal exposure for chlorine gas is 19,000 mg-min/m, and the median incapacitating exposure is 1,800 mg-min/m (U.S. Army et al., 1990). In many parts of the world, other potentially dangerous chemicals are also stored in large above-ground tanks.

Railroad tank cars and tanker trucks also carry a variety of highly toxic chemical agents and reactive intermediate agents for chemical synthesis. These cars and trucks are moving targets of opportunity. The potential release of toxic chemical intermediates from moving or stationary sources continues to be a cause for concern in many parts of the world. The disastrous release of methyl isocyanate near the city of Bhopal, India, in 1984 remains an icon for potential releases from chemical plants that store or use toxic intermediates.

Another source of contamination during deployment might be through U.S. or allied attacks on enemy CB manufacturing or storage

sites. Great care must be taken to identify these locations and assess the potential damage from the release of CB agents. One report stated that NATO briefers showed little regard for the danger of chemical releases during the recent bombings in Serbia. This danger was highlighted by both the Association of Greek Chemists and the Serbian Chemical Society (Heylin, 1999).

Exposures during deployments include not only exposures to agents, but also exposures to chemicals used with military materiel and exposures during off-duty hours. Operational exposures are associated with on-duty performance and may include exposures to chemicals, such as petroleum, oils, and lubricants; cleaning solvents; weapons discharge offgases; smokes and obscurants; and chemicals from nonoperational sources. Off-duty exposures are from ambient and indoor environments away from operational areas. Exposures to pesticides and dust-suppression agents can occur on or off duty. Damaged or nonoperational infrastructures can also be a source of harmful exposures.

Another source of toxic chemicals is the transformation of common industrial chemicals into more toxic species by environmental processes. For example, under certain conditions, parathion, an organophosphate pesticide, can be transformed to paroxon, a much more toxic compound. Many fieldworkers have been poisoned as a consequence of such transformations (Spear et al., 1977). Chemicals can also interact upon exposure to produce toxic effects. For example, reactive air pollutants, such as hydroxyl radicals (commonly found in the atmosphere of most U.S. urban areas), can interact with VOCs and convert them to other chemical compounds. Examples of common transformations can be found in a paper prepared by Yang (in press) for the risk assessment framework component of this study (NRC, 1999a). Unfortunately, given the wide variety of chemicals encountered during deployments, it is difficult to anticipate these interactions. One approach to this problem is to develop a matrix that links VOCs to the products of their transformation.

A common goal of several agencies, such as EPA, the World Health Organization, and OSHA, is to clarify the links between chemical exposures and health effects to protect both occupational and nonoccupational populations. These organizations consider a broad range of health effects, including cancer, reproductive effects, inheritable genetic defects, immunological effects, neurological effects, chromosome aberrations, and respiratory effects, many of which may be the results of cumulative exposures (i.e., from multiple exposure pathways and different chemicals with the same target tissue). For other substances, peak exposures are needed to determine the likelihood of health effects.

During deployments, the military should undertake surveillance of the local use of chemicals, evaluate the effects on military operations, and

keep records of this information. For chemicals commonly used by the military, a great deal of information has already been compiled, similar to the reports prepared by the NRC Committee on Toxicology (COT) on the potential health effects of exposures to fuel vapors (NRC, 1996) and to military smokes and obscurants (NRC, 1997d).

BIOLOGICAL AGENTS

Deployed personnel face potential exposures to harmful biological organisms, both as warfare agents and as endemic organisms, and toxins that can be transferred from air, water, soil, plants, animals, and other people in the theater of deployment. Potential exposures to biological agents have traditionally been much more difficult to detect and monitor than exposures to chemical agents. Often symptoms and patterns of disease can only be assessed *ex post-facto*.

Biological Warfare Agents

Biological warfare agents include both organisms and biological toxins derived from organisms. Organisms that could be used as biological agents include viruses, bacteria, rickettsia, and genetically altered organisms. Biological warfare agents can be disseminated as aerosols, liquids, or powders or can be introduced directly into food or water.

Current biological agents of concern to DoD include viruses, such as eastern equine encephalitis, western equine encephalitis, Venezuelan equine encephalitis, ebola, marburg, rick-borne encephalitis, smallpox, Congo Crimean hemorrhagic fever, junin, lassa, machupo, monkeypox, Rift Valley fever, and yellow fever; bacteria, such as *Bacillus anthracis, Brucella abortus, Brucella melitensis, Brucella suis, Burkholderia mallei, Burkholderia pseudomallei, Francisella tularensis, Yersinia pestis*; and rickettsii, such as *Coxiella burnetti*, *Rickettsia prowazeki*, and *Rickettsia ricketsii*. Table 3-1 provides a summary of diseases, likely pathways of transmission, lethality, and infectivity (i.e., the number of organisms required to cause disease in a healthy adult) associated with selected biological agents. Appendix C describes the characteristics of a number of biological agents.

Biological toxins are harmful chemical compounds produced by living organisms. They come from bacteria, dinoflagellates, algae, molds and fungi, plants, and animals. Some biological agents are highly toxic. Others, such as mycotoxin, poison ivy, and poison oak, attack the skin but are not lethal unless a break in the skin occurs. Biological toxins are often quite stable; are easily taken up on the skin, in the lungs, or in the gut; and produce symptoms that require extensive and rapid medical intervention. Table 3-2 provides summary information on characteristics of a number

of toxins that could be used as warfare agents. The table includes the sources and names of toxins, the LD_{50} based on the route of contact, the concentration corresponding to lethal effects, rates of action, and other relevant factors. The concentration corresponding to lethal effects is derived from the LD_{50} for a 70-kg adult breathing at a rate of 0.016 m/min for 30 minutes or ingesting three liters of water or three kg of food.

A comparison of data shows that the lethal doses for biological toxins are much lower than those for chemical agents. In other words, low concentrations of biological toxins can be much more dangerous to troops than chemical agents. AELs have not been established for biological toxins but are likely to be more than an order of magnitude below lethal chemical levels.

So far, little attempt has been made to set performance goals for detecting biological toxins even though some toxins, such as *Botulinium*, are many times more toxic than chemical agents, even lethal chemicals. Because of their lethality at relatively low doses, biological toxins could pose a threat comparable to the threat of many chemical agents. Detecting and monitoring exposures to life-threatening toxins requires a much more sensitive detection system than detecting and monitoring systems for most chemical agents.

Apparently, DoD has largely discounted the likelihood that toxins will be used against deployed forces. DoD's decisions for developing new detection technologies, however, should be based not only on the likelihood of use but also on lethality. If no strong justification is found for assigning toxins a low priority, then an appropriate level of research should be devoted to methods for detecting and monitoring biological toxins.

Endemic Biological Organisms

Endemic biological microbial organisms exist naturally in the deployment area to which deployed forces would not be immune. These organisms could include airborne microbes and fungi, waterborne microbes and fungi, biological agents in food, and disease organisms transmitted by human contact (Rose, in press).

RELATIONSHIP BETWEEN EXPOSURE AND TOXICITY FOR CHEMICAL AND BIOLOGICAL AGENTS

The prescribed safe doses for chemical agents vary greatly, as do the time-history of concentration and health effects. For some agents, the peak exposure concentration is most important; for others, the number of times the concentration exceeds specified concentration levels or the average exposure concentration exceeds a specified level is the key factor;

TABLE 3-1 Exposure Factors for Selected Biological Warfare Agents

Agent	Disease	Transmission
Bacteria		
Bacillus anthracis	Anthrax	Spores in aerosol
Vibrio cholera	Cholera	Food and water Aerosol
Yersinia pestis	Pneumonic plague	Aerosol inhalation
Franciscella tularensis	Tularemia (rabbit fever)	Aerosol inhalation
Shigelladysenteriae	Dysentery	Inhalation and ingestion
Rickettsia		
Coxiella burnetti	Q fever	Aerosol inhalation Food
Rickettsia rickettsii	Rocky Mountain spotted fever	Vectors
Viruses		
Ebola virus	Ebola	Direct contact Aerosol
Venezuelan Equine Encephalitis (VEE) virus	Encephalitis	Vectors
Yellow fever virus	Yellow fever	Vector/tick
Rift Valley fever virus	Rift Valley fever	Vector/mosquito
Variola virus	Smallpox	Aerosol
Hanta virus	Hanta	Aerosol
Dengue fever	Dengue fever	Aedes mosquito

[a] These numbers were calculated by dividing the infectivity level by 2 m^3 (the amount of air assumed to be breathed in two hours by an active adult) or by 2 L, the amount of water consumed during a day.
Source: Boyle, 1998b.

for still others, the cumulative intake or uptake during a series of exposures is the critical parameter. Dose-response information for chemical agents at low doses and low dose rates is still insufficient for determining safe doses (NRC, 1997c; GAO, 1998).

Because different levels of exposure and concentrations lead to health impacts for different agents, both the frequency and sensitivity with which chemical concentrations must be measured must be carefully defined, especially for low-level exposures. Figure 3-1 shows the variation in the median lethal air exposure, LCt_{50}, and median incapacitating air exposure, ICt_{50}, for a number of chemical warfare agents. This type of toxicity information can provide a basis for setting the performance goals of detection equipment. Protecting against incapacitating effects requires 2 to 10 times more sensitivity than protecting against lethal exposures. Most detection equipment measures concentrations. Unfortunately, there

Lethality	Infectivity	Required Detection Capability[a]
High ~ 100%	10,000 organisms	5,000 org/m^3 air
Low with treatment	1 million organisms	500,000 org/L water
High unless treated	< 100 organisms	50 org/m^3 air
Moderate	1 to 50 organisms	< 25 org/m^3 air
Moderate	10 to 100 organisms	25 org/m^3 air 25 org/L water
Very low	10 organisms	5 org/m^3 air < 5 org/kg food
Low	N/A	N/A
High for Zaire strain	N/A	
Low	N/A	
Low	N/A	
Low	N/A	
High to moderate	N/A	
43% in U.S.	N/A	N/A
Low to moderate	N/A	

is so little reliable information about the threshold effect for biological agents, that determining concentrations can be very risky. Figure 3-2 illustrates the range of sensitivity required for detection/monitoring equipment to protect against a range of health effects. This figure shows how the EC_{50}, the 30-minute average air concentration that would result in the LCt_{50}, compares to the estimated safe dose and to the Surgeon General's AEL. Defining a safe dose, or AEL, requires significantly more sensitivity than defining a lethal or incapacitating dose—in many cases, orders of magnitude more sensitivity.[1]

[1] The AEL, which is designed for controllable conditions, however, may be very different from the safe-dose level on the battlefield.

TABLE 3-2 Characteristics of Selected Biological Toxins

Source	Toxin	LD_{50} (μG/kg)	Required Detection Capability[a]	Notes
Bacteria				
Clostridium botulinium	Botulinium A, B, C, D, E	~ 0.02 (inhalation)	0.1 mg/m^3	Among the most potent toxins known.
		1 (oral)	0.02 mg/L (water or food)	Delayed lethality. Persists in food and water. Breaks down within 12 hours in air.
Clostridium perfringens	Gangrene-causing enzyme	0.1 to 5	0.3 mg/m^3	Delayed action. Low mortality, but very debilitating.
Clostridium tetani	Tetanus toxin	~ 3	N/A	Delayed action. Relatively unstable and heat sensitive.
Cornyebacterium diptheria	Diptheria toxin	0.03	N/A	Lethal. Rapid acting.
Staphylococcus aureus	Staphylococcus enterotoxin A, B, C, D, E (Toxicity is for type B)	0.4 (aerosol ED_{50}) 20 (aerosol LD_{50}) 0.3 (oral ED_{50})	0.058 mg/m^3	Rapid acting. Symptoms persist for 24 to 48 hours. Severely incapacitating.
			3 mg/m^3	Can be lethal. Large-scale production feasible.
			0.007 mg/L	Very stable.
Dinoflagellates				
Gonyaulax tamerensis, Gonyaulax catanella, and related species	Saxitoxin (shellfish poison)	1 (aerosol inhalation) 7 (oral)	0.01 mg/m^3 (air) 0.2 mg/L	Lethal. Rapid acting. Soluble in water. Relatively persistent.
Takifugu poecilonotuss	Tetrodotoxin	1.5 to 3 (inhalation) 30 (oral)	0.3 mg/m^3 (air)	Lethal. Rapid acting.

Algae				
Anacystis species, Anabanea flos-aquae	Anatoxin A (VFDF)	170 to 250 (IP)[b] 5,000 (oral) 2,100 (dermal)	100 mg/L(kg) (water or food)	Very fast death factor. Very rapid acting.
Microcystis aeruginosa, Microcystis, cyanea	Microcystin (FDF)	25 to 100 (IP)[b]	~10 mg/m^3 (air) ~2 mg/L (water)	Lethal, rapid acting. Fast death factor.
Fungi				
Fusarium species	Trichothecene mycotoxins ("yellow rain")	25 to 500 (inhalation) 1,600 (oral)	40 mg/m^3 (air) 40 mg/L	Nonlethal, delayed effects. Inhalation, ingestion, dermal. Very stable. Small repeated doses are cumulative.
Plants				
Ricinus communis	Ricin	1,000	150 mg/m^3 (air) 20 mg/L (water)	Lethal, delayed action. Easily produced. Persistent
Animals				
Palythoa (soft corals)	Palytoxin	0.08 to 0.4	0.035 mg/m^3 (air) 0.006 mg/L (water)	Lethal and rapid acting. Stable
Conus geographus; Conus magnus (fish-hunting cone snails)	Conotoxins	3 to 6	~0.6 mg/m^3 (air) ~0.1 mg/L (water)	Water soluble. Highly stable. Can be used as aerosols. Easily synthesized.
Phyllobates aurotaenia and Phyllobates terribilis (Columbian frog)	Batrachotoxin	0.1 to 0.2	0.015 mg/m^3 (air)	Rapid acting and lethal. Very stable. Can be synthesized.

[a] Assumes 70-kg adult breathing at a rate of 0.016 m^3/min for 30 minutes for air or the ingestion of 3 L water or 3 kg food by a 70-kg adult.
[b] IP refers to intraperitoneal injection dose to mice.

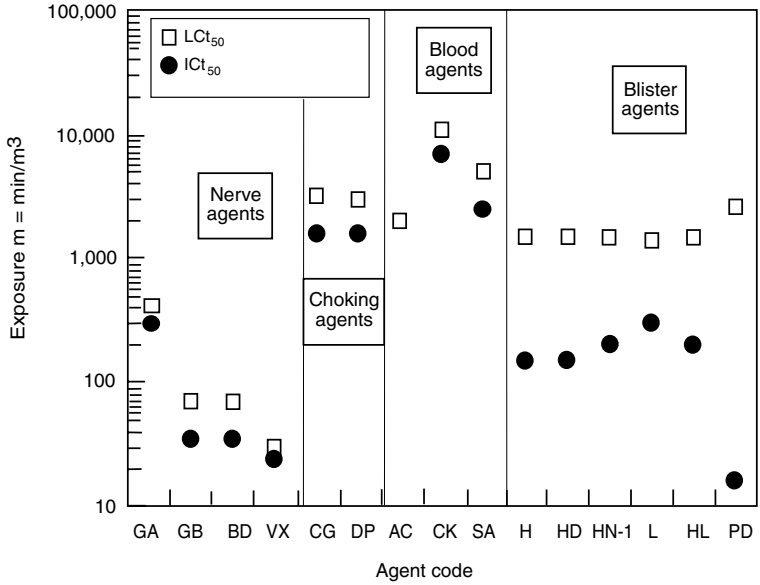

FIGURE 3-1 Variations in the median lethal air exposure, LCt_{50}, and median incapacitating air exposure, ICt_{50}, for some chemical warfare agents.

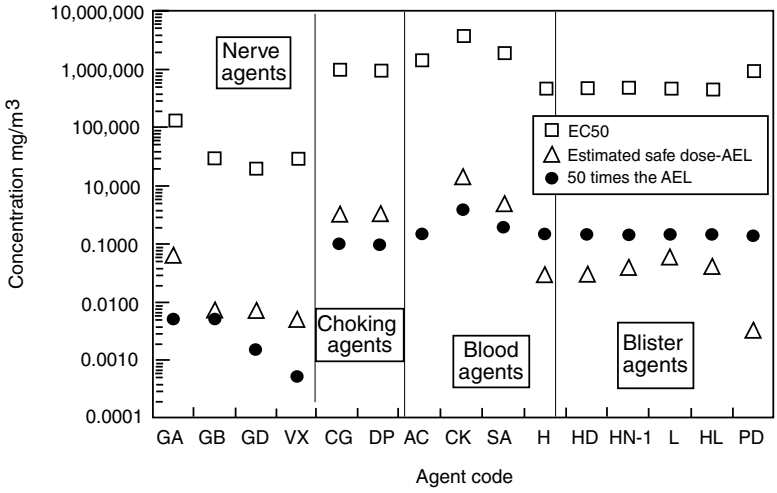

FIGURE 3-2 The EC_{50} (the 30-minute average air concentration that would result in the LCt_{50}) compared to the estimated safe dose and the Surgeon General's AELs.

Sources: Boyle, 1998a; ERDEC, 1996; NRC, 1997c; U.S. Army et al., 1990.

Assessing low-level exposures to a large number of chemicals will require detection and monitoring equipment with a high level of sensitivity and specificity over a broad range of chemical categories. Figures 3-3 and 3-4 show EPA estimated safe air and safe water concentrations for selected TICs. (The derivations of these are discussed in Appendix B.) These numbers are NOT meant to be used as standards by DoD but only to illustrate the level of sensitivity necessary for identifying low-level exposures to TICs.

In fiscal year 1996, DoD dedicated $5 million to evaluating the chronic effects of low-dose exposures to chemical agents (DoD, 1999a). In 1997, studies were initiated to develop highly specific and sensitive assays, preferably forward deployable, to detect and quantify low-level exposures to chemical agents. According to the *Persian Gulf Veterans Coordinating*

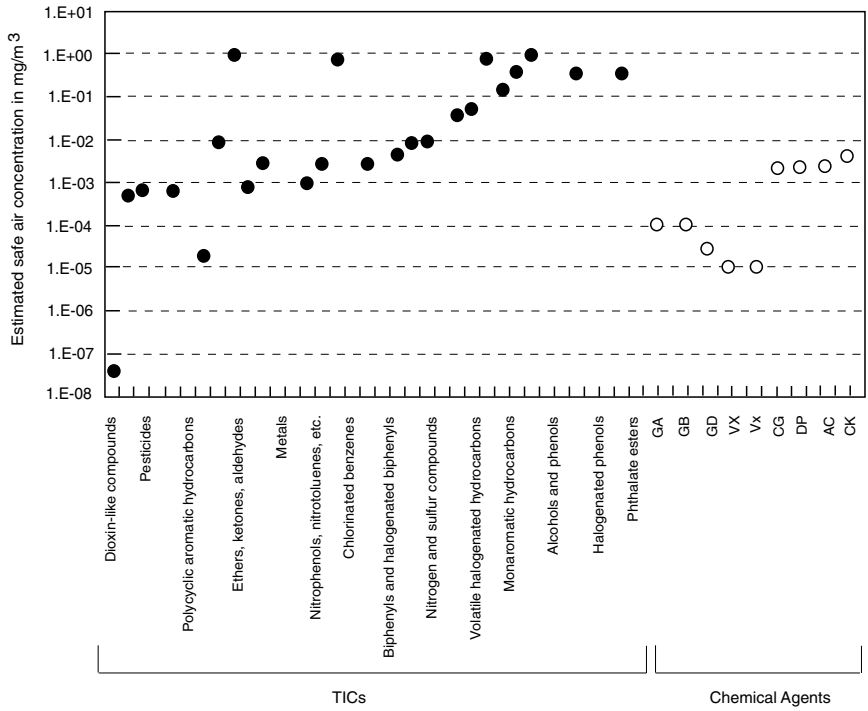

FIGURE 3-3 Estimated safe air concentrations for some TICs regulated by the EPA and some chemical agents. The numbers illustrate the level of sensitivity necessary to identify low-level exposures and should not be used as standards by DoD.

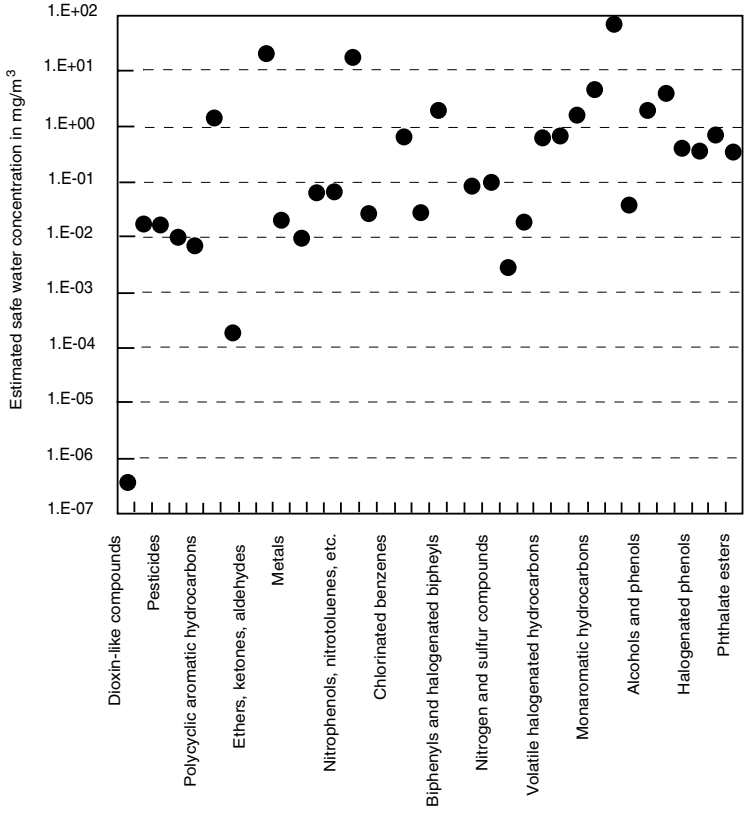

FIGURE 3-4 Estimated safe water concentrations for some TICs regulated by EPA.

Board Action Plan with Respect to the Findings and Recommendations of the Presidential Advisory Committee on Gulf War Veteran's Illnesses (1997, p. 2-3),

> Federal research requests for proposals include the possible long-term health effects of chemical and other hazards (including subclinical exposure to chemical warfare nerve agents) . . . development of a strategic plan [is under way] for research into the potential health consequences of exposure to chemical or other hazards, including low levels of chemical agents.

However these studies will take several years, and improvements can and should be made before then. A starting point for the working definition of low-level concentration could be the low-dose data currently available and the emerging capability of detection equipment.

The U.S. Army Center for Health Promotion and Preventive Medicine (CHPPM) has published Technical Guide 230A, *Short Term Chemical Exposure Guidelines for Deployed Military Personnel*, which can be used to address the potential health risks that may be experienced by deployed military personnel following temporary or short-term exposure to a number of toxic chemicals. The report gives Military Air Guidelines-Short Term and Military Water Guidelines-Short Term for chemical warfare agents, military smokes and obscurants, riot control agents, and TICs. The TICs are ranked according to high, medium, and low priority (U.S. Army CHPPM, 1999). A second technical guidance document (TG 230B) under development will address the risks associated with long-term exposures (i.e., from 14 days to one year).

For biological warfare agents, current DoD estimates of the detection level to protect against infection can be found in the last column of Table 3-1. Ideally, however, much greater detection sensitivity would provide a margin of safety before an area is declared free of biological agents. A first step toward more sensitive assessments and models of dose-response relationships would be to determine their feasibility. Methods developed by epidemiologists, toxicologists, and biostatisticians for chemicals would be a logical starting point.

FINDINGS AND RECOMMENDATIONS

Finding. Because little information is currently available relating long-term health effects to low-dose or low-dose-rate exposures to chemical agents, it is extremely difficult to set performance criteria for detecting and monitoring concentrations of these agents. As a starting point for a working definition of low-level concentration, DoD could use the low-dose data currently available and the capability of available detection equipment.

Recommendation. The Department of Defense (DoD) should increase its efforts to collect and evaluate individual and group dose-response data for a broad set of chemical warfare agents. Studies could include standard animal toxicity testing protocols for long-term effects, as well as retrospective epidemiological studies on individuals exposed to these substances in their occupations. DoD should use the detection capability of available equipment as its working definition of low-level concentration.

Finding. In addition to chemical warfare agents, thousands of TICs are in or are brought into the theater of deployment. These chemicals include pesticides, fuels, paints, and lubricants. Under combat conditions,

existing controls and safety precautions may not be practical. Storage tanks, production facilities, pipelines, and other equipment may be damaged, for example, and the TICs dispersed. Exposure under these conditions may be uncontrolled, unreported, unrecorded, and extremely dangerous. Exposures could have long-term health effects that cannot be easily distinguished from the long-term health effects of low-level exposures to chemical warfare agents.

Detecting and monitoring exposures continually to the full set of toxic chemicals would be extremely difficult, if not impossible. Toxicity data for a number of TICs being developed by some government agencies, such as the EPA and OSHA, are being reviewed by independent groups, such as the NRC COT. The data, thus far, show large variations in toxicity.

Recommendation. The Department of Defense should review its current efforts to catalog and prioritize toxic industrial chemicals. This information should be used to anticipate the types of chemicals that may be encountered during a deployment and to prioritize them.

Finding. Very little information is currently available to relate long-term health effects to low-level exposures to biological agents. Almost no information is available on how combined or sequential exposures to low levels of CB agents can affect the short-term or long-term health of troops. Until DoD can accumulate and analyze information on low-level exposure or dose response, as well as on long-term chronic effects, it will be very difficult to set performance criteria for detecting and monitoring concentrations of CB agents for assessments of long-term health effects. Potential interactions among agents, which can be cumulative, synergistic, or antagonistic, add to the difficulty. For example, chemical interactions may, in fact, abate, or even destroy, a biological agent. In fact, at one time, DoD research was focused on using a chemical agent to counter a biological agent cloud.

Recommendation. The Department of Defense should increase its efforts to collect and evaluate low-level dose-response data for a broad set of biological agents. The data should include information on the infectivity of a range of both warfare and endemic biological agents. At the same time, studies should be undertaken to determine whether and which combined chemical and/or biological agent exposures should be investigated. This information should be used to define a strategy for monitoring exposures to multiple biological agents.

Finding. Current criteria for detecting CB warfare agent concentrations are designed to prevent exposures to lethal and incapacitating levels.

Often the only way to determine if individuals have been affected by exposures to harmful agents is if they have immediate symptoms. Thus, data are not provided in a form that can be used to establish or verify retrospectively the health effects of CB agents over the long term.

Recommendation. The Department of Defense should establish a plan to collect data for all types of potential agent exposures to identify potential or emerging medical problems quickly. If possible, these medical problems should then be evaluated in terms of any prior exposures to chemical and/or biological warfare agents that have been associated with that health outcome. This plan should include guidelines for who should get the information and when they should receive it.